Walter Reed Army Institute of Research
Standard Operating Procedure

SOP Title:	**Scientific Review of Human Use Protocols**	SOP No.	**UWZ- 002**
		Version	**.01**
Effective Date	15 May 2014	Page	**1 of 9**

Signatures and Dates:

Author(s)	Signature on file at HSPB Maryanne T. Vahey, Ph.D. Science Director	20 May 2014 Date:
Approving Authority	Signature on file at HSPB Steven E. Braverman COL, MC WRAIR Commander	22 May 14 Date:

Review/Approval for unchanged documents

Date	Author	QA Review	Approving Authority

1. Purpose/Applicability

This document articulates the scientific review process for human subjects research protocols mandated under AR 70-25, 32 CFR 219, and DoDI 3216.02.

The establishment of a standing Scientific Review Committee (SRC) is outlined in WRAIR Policy Letter 2014-26.

This standard operating procedure applies to the WRAIR Science Director (SD), the SRC Chair, SRC Members, the Human Subjects Protection Branch (HSPB), Branch, Program and Center Directors (will be referred to hereafter as Directors) and Investigators to include all persons covered under the WRAIR Human Research Protection Program (HRPP).

2. Responsibilities

a. The WRAIR Commander is responsible for appointing members of the SRC. He/she may delegate this responsibility.

b. Directors are responsible for:
   1) identifying researchers to serve on the SRC.
   2) evaluating protocols prior to submission to ensure that they are complete, mission aligned, and sufficiently mature to begin the review process.

c. HSPB is responsible for:
   1) determining if an amendment requires scientific review.
   2) maintaining all records associated with the scientific review along with all other records and documentation pertaining to the protocol.

d. The SD is responsible for:
   1) determining if extramural reviews are acceptable. The WRAIR will accept scientific reviews from the Armed Forces Research Institute for Medical Science (AFRIMS), the Naval Medical Research Center (NMRC) and the Protocol Scientific Review Committee (PSRC) at the National Institute of Allergy and Infectious Diseases (NIAID) without additional review.
   2) coordinating the participation of external reviewers when specialized expertise is required for protocols.
   3) mediating disagreements between the SRC and an Investigator in the case of an impasse.

4) determining if an effective mitigation plan is required to address a potential conflict of interest for a SRC Member.

e. The Chair of the SRC is responsible for:
1) convening the Scientific Review Committee (in person or electronically) and managing the review process with the Investigator.
2) assuring that the appropriate subject matter experts are reviewing the scientific aspects of the protocols.
3) determining the role each committee member shall serve for each protocol review.
4) assisting the SD with mitigation plans for potential conflicts of interest.
5) maintaining a list of alternate reviewers by subject matter expertise should a conflict of interest arise.
6) collating the comments from the members of the Scientific Review Committee and confirming that the comments adhere to the SRC SOP
7) reconciling and documenting disparate opinions within the SRC and formulating the final requirements and recommendations from the review.
8) communicating results of the review and any subsequent amendments to the SD within 3 business days following completing the review.
9) determining if an Investigator's request to extend a timeline is justified and the length of the extension. This must be communicated to the SD.
10) informing HSPB when a protocol has been approved (via email) and placing the final version of the protocol on the V drive folder along with all associated correspondence and the approval memorandum.
11) maintaining a hard copy set of credentials for all SRC members to consist of an up to date curriculum vita and required training certification.
12) conducting training for SRC members which will consist of an orientation for all new members and an annual refresher for the standing SRC.

f. SRC Members are responsible for:
1) ensuring receipt of protocol packets.
2) immediately informing the SRC Chair and the SD if a conflict of interest exists for the review of a protocol.
3) immediately informing the SRC Chair and the SD if an SRC member appointed for review will be unavailable (TDY, etc.) to complete the review within the required suspense date.
4) reviewing the protocol packet in accordance with this SOP.

5) attending Committee meetings and sharing their comments/evaluation with the Committee. Members should have their comments and recommendations prepared prior to Committee meetings.
6) evaluating revisions made by Investigators and communicating to the Committee Chair whether the revisions meet the intent of the requirements defined in the previous review.

g. The Investigator is responsible for:
1) submitting the protocol to HSPB as outlined WRAIR Policy 12-05.
2) Identifying an alternate corresponding Investigator for all regulatory matters in event the PI is not available.
3) responding to the SRC Chair for clarifications and minor issue resolution.
4) making changes to the protocol as required by the SRC within 10 business days of receipt of the review. The Investigator should notify the Chair of the SRC if the revisions cannot be made within the expected timeframe.
5) submitting the final scientifically approved protocol to the HSPB. Electronic submission process: one new revised document with tracked changes and the same new revised document without tracked changes.
6) managing protocol document version control. This may be in accordance with Sponsor mandated conventions.

3. Material and Equipment

N/A

4. Procedures

a. The SRC members are appointed by the Commander of WRAIR. The SD and SRC Chair provide the Commander recommendations for members based on information provided by the Directors. All scientific staff members are required by HQ, WRAIR, to participate as assigned on the SRC as a part of their job responsibilities. SRC members will serve for a period of 12 months with a staggered rotation.

b. To ensure the integrity and quality of the scientific review process, proposed members must be experienced in the conduct of human use research at the Investigator level, including drafting of human use protocols, submission to HSPB, execution, and drafting of clinical study reports and/or publication of results. This experience should be documented by the Director.

c. Scientific review will be performed by a standing committee of members who are assigned for at least twelve months with a staggered rotation. The Committee will minimally consist of a Chair and at least four other Investigators. The membership should reflect broad diversity in experience and expertise. The Committee Chair should be a senior scientist; an O6 for active duty or a DB 4 (GS 15 equivalent) for civilians. The Chair may delegate responsibility to another qualified member. Additional committee members may be designated with subject matter expertise as requested by the committee chairperson or SD. A Non-voting statistical subject matter expert will provide proper review of the statistical analysis algorithm and power estimations. Alternatively, the statistician may be appointed to the SRC as a voting reviewer.

d. Protocols are submitted from WRAIR Directors with a cover memo from the Investigator to which the Director or designee appends an acknowledgement that he/she approves the protocol quality, deems it to be of scientific merit, and confirms it is mission relevant (WRAIR Policy 12-05). The protocol is submitted to the HSPB following the regulatory guidelines articulated in 32 CFR 219.

e. The HSPB confirms that a protocol is human subjects research, ensures that the submission contains all required elements and it is properly organized and formatted and forwards the protocol package to the Chair, SRC, to coordinate scientific review, with a copy to the SD. WRAIR accepts the reviews conducted by AFRIMS, NMRC and the PSRC at NIAID without additional scientific review. For all other submissions, if a protocol has received an external scientific review, HSPB forwards the protocol package to the SD for a concurrence and/or establishment of an additional scientific review. HSPB should complete this evaluation within 3 days of receipt unless there are extenuating circumstances or complexities in which case HSPB would document the reason for delay.

f. Amendments to protocols are submitted from Investigators with a cover memo in which the Director (or designee) acknowledges he/she concurs that the amendment is appropriate for the research, is militarily relevant, appropriately resourced, etc. The amendment is submitted to the HSPB following the regulatory guidelines articulated in 32 CFR 219. HSPB evaluates the amendment and forwards those that require a scientific review to the SRC Chair to coordinate the scientific review, with a copy to the SD. WRAIR will accept amendments already reviewed by AFRIMS, NMRC and the PSRC at NIAID without further scientific review. All other

amendments that have received an external scientific review, are forwarded to the SD for concurrence or an additional scientific review. HSPB should complete this evaluation within 3 days of amendment receipt.

g. The SRC Chair will log receipt of packets from HSPB into the electronic SRC data base on the V drive. The day of receipt is considered Day 0 of the scientific review process. If a protocol or amendment has received an external scientific review, the SD will determine if the external scientific review is sufficient to meet the intent of AR 70-25, DODI 3216.02, 32 CFR 219. If not, the package will be submitted through the standard process (see Appendix B). The SD will complete this determination within three business days and notify HSPB and the Investigator of the outcome. This timeline assumes that the external scientific approval is attached and that there are no issues complicating the decision in which case this timeline will be extended until such issues are clarified.

h. If there has been no previous scientific review, the SRC Chair receives the protocol or amendment directly from the HSPB, with a copy furnished to the SD. If, in the case of a protocol or amendment that has received external scientific review, a WRAIR scientific review is deemed necessary by the SD, the protocol or amendment package is forwarded by the SD to the SRC Chair by the next business day subsequent to the determination. The SRC Chair determines which members will review the packet based on the protocol subject matter and identifies and addresses conflict of interest or scheduling/availability issues for any of the reviewers. The Chair forwards the packet to the vetted reviewers and notifies the SD and the Investigator. A minimum of three members review any one protocol. A Chair may elect to review amendments without additional input from other members.

i. The Chair will manage the style of the scientific review, communicating with the Investigator by email at the start of the review process. Complete review by all designated committee members is required. The Chair will prepare the final summary of the review for the Investigator. The Chair is the final authority for identifying which revisions are required and which are merely recommended. Although the Chair has final authority within the Committee, Chairs are expected to respect the opinions of all Committee members and give appropriate consideration to their judgments. Members will provide reports of their review to the Chair within seven business days.

j. The Chair must provide a report of the review to the Investigator, with a copy furnished to the SD within 10 business days of receipt of the protocol packet, unless there are documented extenuating circumstances. The report should state whether the protocol is approved, approved with revisions, or disapproved, and the basis for these judgments. The report must clearly identify what version of the protocol and what other documents were reviewed for this report.

k. The SRC Chair logs receipt of the review. The Investigator must respond to the review within 10 business days or request a delay. The Chair will determine whether the delay is justified and determine a reasonable new suspense date. If the Investigator does not respond within the specified period, the protocol will be withdrawn. The SRC Chair will generate a withdrawal memo and forward it to the Investigator with a copy provided to the Investigator's Director and the HSPB. If an Investigator chooses to withdraw a project from the Scientific Review process, he/she will submit a memo/formal email through the Director to SRC Chair requesting that the review process be stopped. The existing scientific review file, including the withdrawal memo and any resulting review documents will be transferred to the HSPB by the SRC Chair and maintained permanently following the withdrawal of the protocol.

l. The Investigator provides a revised packet to the SRC Chair who logs its receipt. Along with the revised protocol, the packet should include a cover memo, approved by the Director, which details the responses to issues identified in the review along with any other changes made since the previous review. The revised document should clearly indicate the new version number and date.

m. The SRC Chair may elect to evaluate the revisions himself/herself or with additional members of the SRC. Review of the revisions by the Chair must ensure that the revisions adequately address the required issues previously identified. All changes should be reviewed for scientific validity.

n. Memoranda sent from the SRC Chair to Investigators will clearly identify which protocol is the subject of the memo using the title, the Investigator, the version, and the submission date. Approval and disapproval memos are written by the Chair of the SRC and will state that the protocol is approved, approved pending required revisions, or disapproved. Reasons for disapproval must be clearly summarized. Memos/emails for administrative withdrawals of protocols from the SRC process are sent to

the Investigator by SRC Chair through the SD and Director, with a copy furnished to the HSPB.

o. The SRC Chair may call for an ad hoc meeting of the SRC at any time.

5. Explanation of Abbreviations and Terms

SD	Science Director
Conflict of Interest	Any condition which could influence an individual to act in a manner that is not in the best interest of the organization. See WRAIR Policy Letter # 08-05 and SOP UWZ-C-609.
Human subjects research	Research involving humans as research subjects, or involving biological specimens, data, specimens from repositories or anatomical substances of human origin, and databases. This includes the administration of questionnaires or surveys, as well as research done in an educational setting.
HSPB	The Human Subjects Protection Branch which supports the WRAIR IRB.
IRB	WRAIR Institutional Review Board or IRB, the ethical review committee for research involving human subjects at WRAIR, its CONUS detachments or OCONUS Laboratories, or when WRAIR funding, facilities or personnel are involved in any way (Investigator, consultant, collaborator, etc.). This includes protocols for which recruitment of subjects is being performed at WRAIR even though the research is conducted elsewhere. See WRAIR Human Research Protection Plan (HRPP).
Protocol Packet	The protocol packet is comprised of the protocol, a draft of the consent forms (if available), draft of the Investigator's brochure

	(if available), and a memo from the Division Director or designee.
Research	Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.
SRC	Scientific Review Committee. This is a standing committee whose members are appointed for 12 months of service.
WRAIR	Walter Reed Army Institute of Research

6. References

Regulation No, SOP etc, if applicable	Document Title
AR 70-25	*Use of Volunteers as Subjects of Research, 25 January 1990*
DODI 3216.02	
32 CFR 219	

7. Forms and Appendices

Form or Appendix Number	Title
Appendix A	SRC Checklist
Appendix B	Algorithm for Scientific Review Process
Appendix C	Approval Memo
Appendix D	Withdrawal Memos

Scientific Review Committee Checklist

The human use protocol (entitled XYZ, PI: ABC) has been reviewed by the scientific review committee members identified below for following items:

	YES	NO
1. The rationale for the study is clearly stated and is scientifically sound.		
2. The hypothesis or study aims are clearly stated.		
3. The objectives or outcomes are clearly defined.		
4. There are adequate preliminary data in the protocol to justify the proposed research.		
5. An adequate literature review has been done to support the study.		
6. The question or hypothesis being tested is of sufficient scientific merit to justify the clinical trial		
7. The design of the study is appropriate.		
8. The validity and reliability of proposed tests have been established or there are methods proposed for establishing validity and reliability.		
9. The proposed subject population is appropriate.		
10. Statistical considerations, including sample size and statistical analysis, are clearly described and adequate.		
11. The proposed tests are required to answer the study objectives.		
12. The principal and all other Investigators are qualified to conduct this study.		

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Reviewer 1 required (signature) print name Date

_____

Reviewer 2 required (signature) print name Date

_____

Reviewer 3 required (signature) print name Date

Algorithm for the Scientific Review Process

A simultaneous review of the protocol by the SRC and the IRB may take place as per the concurrence of the HSPB and the SD.

Standard Process (maximum timeline)

Business Day minus 3
: Investigator submits protocol package to HSPB

Within 3 Business Days
: HSPB determines if project is human subjects research and estimates risk level. The SRC and SD will only receive the protocol if it is minimal risk or greater than minimal risk and requires a review or if the principal Investigator of an exempt protocol is also the Director (a conflict of interest).

Day 0
: HSPB forwards the protocol package to the Chair, SRC, for Scientific Review (Email and saved on the V:/), Copy to SD.

Business Day 1
: Chair, SRC, determines members that will review protocol and notifies SRC, and forwards protocol package to assigned members

Business Day 2 through 10
: The SRC reviews protocol with Investigator, prepares comments, and provides the Protocol Package with the comments to the Investigator, with a copy of comments to the SD

Business Day 11 to 20
: The Investigator responds to the scientific review and returns the revised Protocol Package to the Chair, SRC, with a copy to the SD.

Business Day 21
: Chair confirms that revisions meet Committee's intent and sends a written Scientific Review approval memo to the Investigator with a copy to the SD as an attachment to an email. If the revisions do not meet the Committee's intent, Chair notifies the Investigator of deficiencies and 10 day response cycle repeats copy to SD.

Business Day 22
: The chair of the SRC forwards the approval and the Protocol Package to HSPB for submission to the ethical review process.

Review of Protocol Packages With Prior Scientific Review and Approval

Business Day Minus 3

Investigator Submits Protocol Package to HSPB

Within 3 Business Days

HSPB determines if project is human subjects research and estimates risk level

Day 0

HSPB Forwards the Protocol Package to SD for Scientific Review for concurrence/non-concurrence.

The SD accepts or rejects the previous scientific review

Business Day 3

If deemed acceptable, the SD provides approval memo to HSPB. The protocol proceeds through ethical review process.

If not acceptable, the Protocol Package is submitted for review through the standard SRC process.

In the Event of an Impasse

The SD will take the initiative to resolve the impasse to include assigning the protocol to a second SRC.

Suspense Dates

Investigators must respond to the SRC within 10 days of receipt of the SRC's review or the protocol will be considered withdrawn. A written withdrawal memo will be generated by the Chair of the SRC and forwarded to the Investigator as an attachment to an email message.

Approval Memo from Scientific Review Committee Chair

MRMC-UW(X-X) (DATE)

MEMORANDUM FOR Maryanne T. Vahey, Ph.D., Science Director, Walter Reed Army Institute of Research, 503 Robert Grant Ave., Silver Spring, MD 20910-7500

SUBJECT: Scientific Review of a Human Subjects Research Protocol

1. As Chair of the Scientific Review Committee (SRC), I have overseen review of the new WRAIR research protocol (or amendment to the research protocol) entitled " " (WRAIR #), (Version & Date), submitted by (PI NAME and contact information).

2. The reviewers for this protocol and their contact information are: XXX

3. All changes requested by the SRC have been made to the committee's satisfaction. (summary finding is below).

4. As Chair of the SRC I approve the scientific merit and approach of this protocol

5. The point of contact for this action is the undersigned.

SIGNATURE BLOCK

1. Withdrawal of Protocol by the Science Director

MRMC-UW(X-X) (DATE)

MEMORANDUM THRU Director, Division of XX, Walter Reed Army Institute of Research, 503 Robert Grant Ave., Silver Spring, MD 20910-7500

FOR Principal Investigator, Division of XX, Walter Reed Army Institute of Research, 503 Robert Grant Ave., Silver Spring, MD 20910-7500

SUBJECT: Withdrawal from Scientific Review of a Human Subjects Research Protocol

1. On (date), the Chair of the Standing Scientific Review Committee (SSRC) overseeing review of the new WRAIR research protocol (or amendment to the research protocol) entitled " " (WRAIR #), (Version & Date), submitted by (PI NAME and contact information) requested protocol revisions. No response has been received from you by the suspense date of (date). This protocol is withdrawn from consideration in accordance with WRAIR SOP UWZ-002, effective 16 June 2008. A new protocol must be submitted to the HSPB if you want to implement this research.

2. The point of contact for this action is the undersigned.

CF: HSPB

MARYANNE T. VAHEY, Ph.D.
SCIENCE DIRECTOR

2. Withdrawal of Protocol from Scientific Review by Principal Investigator

MRMC-UW(X-X) (DATE)

MEMORANDUM THRU Director, Division of XX, Walter Reed Army Institute of Research, 503 Robert Grant Ave., Silver Spring, MD 20910-7500

FOR WRAIR Chair, Scientific Review Committee, Walter Reed Army Institute of Research, 503 Robert Grant Ave., Silver Spring, MD 20910-7500

SUBJECT: Withdrawal from Scientific Review of a Human Subjects Research Protocol

1. I request withdrawal from review of WRAIR research protocol (or amendment to the research protocol) entitled " " (WRAIR #), (Version & Date), submitted by (PI NAME and contact information) on (date). This protocol is withdrawn from consideration in accordance with WRAIR SOP UWZ-002, of 16 June 2008.

2. The point of contact for this action is the undersigned.

CF: HSPB

SIGNATURE BLOCK